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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/758,036	01/11/2001	Ekkehard Leberer	38005-0126	8288

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EXAMINER

JOIKE, MICHELE K

ART UNIT	PAPER NUMBER
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1636

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

09/758,036

Applicant(s)

LEBERER ET AL.

Examiner

Michele K. Joike, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 November 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4-10,20 and 21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2, 4-10, 20 and 21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Receipt is acknowledged of a reply to the previous Office Action, filed November 15, 2006. Amendments were made to the claims.

Claims 1-2, 4-10, and 20-21 are pending in the instant application. Claims 3, 11-19 and 23-25 are canceled. Any rejection of record in the previous Office Action, mailed April 13, 2006 that is not addressed in this action has been withdrawn.

Because this Office Action introduces new rejections other than those set forth in the previous Office Action, and are not necessitated by amendment, this Office Action is **Non-Final**.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4 and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 recites the process of claim 1 wherein the human potassium channel is Kv1.5 or gplRK1. gplRK1 is a guinea pig potassium channel, and therefore cannot be a human potassium channel.

This new rejection is necessitated by amendment.

Response to Arguments Concerning Claim Rejections – 35 USC § 103

Applicant's arguments filed November 15, 2006 have been fully considered and they are persuasive.

The following grounds of traversal are presented:

Applicants argue that the only reference that teaches a human potassium channel is Rampe et al, and they use human cells, and do not teach using yeast mutant cells. Tang et al teaches a guinea pig channel in a yeast double mutant; Gaber teaches a plant potassium channel in a yeast double mutant; and, Ketchum et al and Fairman et al do not teach yeast mutants complemented with non-yeast genes. None of these references teaches or suggests a yeast triple mutant that is complemented by a human potassium channel.

Since these arguments are found to be persuasive, the previous rejections under 35 USC § 103(a) are withdrawn, and a new 35 USC § 103(a) rejection is made below. This new rejection is not necessitated by amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 2, 6 –10, 20 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over US20030165806 (hereinafter Pausch) in view of US 5,795,770 (hereinafter Gaber) in further view of Fairman et al.

The claims are drawn to a process for identifying inhibitors or activators of a human potassium channel using mutant *S. cerevisiae* cells with inactivated endogenous potassium channels TRK1, TRK2 and TOK1, which is not complemented by an expressed HERG1, and wherein a human heterologous potassium channel is expressed in the mutant cell. The inhibitor or activator is added to the mutant cells and the effect of the inhibitor or activator is determined. The human potassium channel is present on a yeast expression plasmid and the yeast cell expresses a growth reporter. Inhibition of growth is determined by measuring the cell count via fluorescence. In claim 21, an inhibitor and substance are both added to the mutant cells and the effect of the substance, as an activator, is determined.

Pausch (US 20030165806, specifically paragraph 82 and Example 15, filing date March 11, 1997) teaches hORK1 (a human potassium channel) in a yeast expression vector transformed into a yeast strain with a TRK1 deletion. hORK1 was expressed under control of the ADH1 promoter. It also teaches screening assays for both agonists and antagonists of heterologous potassium channels. The yeast strains transformed with hORK1 were examined for their ability to grow on low potassium media. Inhibitors were added to determine if potassium channels were blocked. (None of the references expresses HERG1.)

Pausch does not teach using mutant *S. cerevisiae* cells with inactivated endogenous potassium channels TRK1, TRK2 and TOK1, determining if a substance activates the potassium channel or measuring the cell count via fluorescence.

Gaber (see especially the abstract, summary and columns 4 and 6-7) teaches a process for identifying inhibitors or activators of a eukaryotic potassium channel using mutant *S. cerevisiae* cells with inactivated endogenous potassium channels TRK1 or TRK1 and TRK2 and wherein a eukaryotic heterologous potassium channel is expressed in the mutant cell. The inhibitor or activator is added to the mutant cells and the effect of the inhibitor or activator is determined. A substance (such a potassium) may be added in addition to an activator to determine the effect of the substance on the cells in the presence of the activator. Large amounts of potassium activated the potassium channel, despite presence of an inhibitor (Example 1). A spectrophotometer is used to count cells. Gaber suggests using human potassium channels in the process.

Gaber does not teach that the mutant *S. cerevisiae* cells were inactivated for TOK1.

Fairman et al (J. Membrane Biol. 168: 149-157, 1999, specifically materials & methods) teach a triple knockout mutant (*trk1Δ trk2Δ tok1Δ*) of *S. cerevisiae*.

The ordinary skilled artisan, desiring to use a process for identifying inhibitors or activators of a human potassium channel using mutant *S. cerevisiae* cells with inactivated endogenous potassium channels TRK1 or TRK1 and TRK2 and wherein a human heterologous potassium channel is expressed in the mutant cell, would have

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been motivated to combine the teachings of Pausch teaching a method of screening for inhibitors using hORK1 (a human potassium channel) in a yeast expression vector transformed into a yeast strain with a TRK1 deletion, with the teachings of Gaber, teaching process for identifying inhibitors or activators of a eukaryotic potassium channel using mutant *S. cerevisiae* cells with inactivated endogenous potassium channels TRK1 or TRK1 and TRK2 and wherein a eukaryotic heterologous potassium channel is expressed in the mutant cell, with the teachings of Fairman et al teaching a triple knockout mutant (*trk1Δ trk2Δ tok1Δ*) of *S. cerevisiae* because Gaber teaches that the beneficial and desirable feature of the mutant *S. cerevisiae* cells was their inability to transport potassium into *S. cerevisiae* cells, and Fairman et al. both taught that TOK1 was a potassium transport channel which was capable of transporting potassium into cells. Therefore, given that TOK1 is a potassium uptake transporter, one of skill in the art would be motivated to inactivate a known potassium uptake transporter in *S. cerevisiae* cells, namely, TOK1 to produce mutant *S. cerevisiae* cells with inactivated endogenous potassium channels TRK1, TRK2 and TOK1 to practice the method of identifying activators and inhibitors of heterologous potassium channel uptake transporters in mutant *S. cerevisiae* cells. It would have been obvious to one of ordinary skill in the art to use a human potassium channel in a yeast triple knockout strain because Pausch teaches that expression of potassium channels from heterologous species in genetically modified yeast are useful in the discovery of human therapeutics. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary,

that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over US20030165806 (hereinafter Pausch) in view of US 5,795,770 (hereinafter Gaber), in view of Fairman et al, and in further view of Rampe et al.

Claim 4 recites that the human potassium channel is Kv1.5.

Pausch, Gaber and Fairman et al teach the limitations as described above.

Rampe et al (J. of Pharmacology and Exptl. Therapeutics 286: 788-793, 1998, specifically the abstract, introduction and the figures) teach the human potassium channel Kv1.5.

The ordinary skilled artisan, desiring to use a process for identifying inhibitors or activators of a Kv1.5 using mutant *S. cerevisiae* cells with inactivated endogenous potassium channels TRK1 or TRK1 and TRK2 and wherein a Kv1.5 is expressed in the mutant cell, would have been motivated to combine the teachings of Pausch teaching a method of screening for inhibitors using hORK1 (a human potassium channel) in a yeast expression vector transformed into a yeast strain with a TRK1 deletion, with the teachings of Gaber, teaching process for identifying inhibitors or activators of a eukaryotic potassium channel using mutant *S. cerevisiae* cells with inactivated endogenous potassium channels TRK1 or TRK1 and TRK2 and wherein a eukaryotic heterologous potassium channel is expressed in the mutant cell, with the teachings of Fairman et al teaching a triple knockout mutant (*trk1Δ trk2Δ tok1Δ*) of *S. cerevisiae*, and with Rampe et al teaching the Kv1.5 human potassium channel because Gaber teaches

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that the beneficial and desirable feature of the mutant *S. cerevisiae* cells was their inability to transport potassium into *S. cerevisiae* cells, and Fairman et al. both taught that TOK1 was a potassium transport channel which was capable of transporting potassium into cells. Therefore, given that TOK1 is a potassium uptake transporter, one of skill in the art would be motivated to inactivate a known potassium uptake transporter in *S. cerevisiae* cells, namely, TOK1 to produce mutant *S. cerevisiae* cells with inactivated endogenous potassium channels TRK1, TRK2 and TOK1 to practice the method of identifying activators and inhibitors of heterologous potassium channel uptake transporters in mutant *S. cerevisiae* cells. It would have been obvious to one of ordinary skill in the art to use a human potassium channel in a yeast triple knockout strain because Pausch teaches that expression of potassium channels from heterologous species in genetically modified yeast are useful in the discovery of human therapeutics. Furthermore, Rampe et al. teach that it is desirable and useful to study the action of heart muscle potassium channels, and to study the action of inhibitors and activators of heart muscle potassium channels. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

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under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Allowable Subject Matter

No claims are allowed.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele K. Joike, Ph.D. whose telephone number is 571-272-5915. The examiner can normally be reached on M-F, 9:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Michele K Joike, Ph.D.
Examiner
Art Unit 1636


NANCY VOGEL
PRIMARY EXAMINER